Complete Summary

GUIDELINE TITLE

Clinical practice guidelines for managing dyslipidemias in chronic kidney disease.

BIBLIOGRAPHIC SOURCE(S)

National Kidney Foundation. Clinical practice guidelines for managing dyslipidemias in chronic kidney disease. Am J Kidney Dis 2003 Apr;41(4 Suppl 3):S1-91. [452 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Dyslipidemias
- Chronic kidney disease

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nephrology
Nutrition
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Dietitians
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide guidelines for the assessment and treatment of dyslipidemias in patients with chronic kidney disease, irrespective of the underlying cause of the kidney disease

TARGET POPULATION

- Adults (≥18 years of age) and adolescents (from onset of puberty to 18 years of age) with Stage 5 chronic kidney disease (CKD)
- Kidney transplant recipients

Note: The Work Group concluded a priori that the Adult Treatment Panel III (ATP III) Guidelines were generally applicable to patients with Stages 1–4 CKD.

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Complete fasting lipid profile with total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides
2. Evaluate for remediable, secondary causes

Management/Treatment

1. Patient Education on therapeutic lifestyle changes:
    - Diet
        - Emphasize reduced saturated fat
        - Emphasize components that reduce dyslipidemia (e.g., fiber)
        - Emphasize total calories to attain/maintain standard National Health and Nutrition Examination Survey (NHANES) body weight
    - Physical activity
        - Moderate daily lifestyle activities
        - Moderate planned physical activity

- Habits
    - Alcohol in moderation
    - Smoking cessation

2. Medication
    - Statins*: pravastatin, lovastatin, atorvastatin**, simvastatin, fluvastatin
    - Fibrates: bezafibrate, clofibrate, ciprofibrate, fenofibrate, gemfibrozil
    - Bile acid sequestrants: colestipol, cholestyramine, colesevelam
    - Nicotinic acid

*Note: These are the statins approved for use in the U.S. by the U.S. Food and Drug Administration

**Note: Atorvastatin is the only statin approved by the U.S. Food and Drug Administration for use in children.

MAJOR OUTCOMES CONSIDERED

Assessment of Dyslipidemias

- Prevalence of dyslipidemias in chronic kidney disease (CKD)
- Association between dyslipidemias and atherosclerotic cardiovascular disease
- Association between dyslipidemias and CKD progression

Treatment of Dyslipidemias

- Efficacy of treatment
- Safety of treatment
    - Pharmacokinetics of lipid-lowering medications in CKD
    - Drug interactions in CKD
    - Adverse reactions to lipid-lowering therapies in CKD

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Work Group collaborated with a professional Evidence Review Team to identify and summarize pertinent literature. The Work Group and the Evidence Review Team first identified the topics to be searched, and the Evidence Review Team conducted the literature search. The topics that were selected for search included the incidence or prevalence of dyslipidemia, the association of dyslipidemia with atherosclerotic cardiovascular disease (ACVD), and the treatment of dyslipidemia in patients with Stage 5 chronic kidney disease (CKD) (including kidney transplant recipients). For patients with Stages 1–4 CKD, topics for the literature retrieval were limited to adverse effects of dyslipidemia treatment, the effects of dyslipidemia treatment on kidney disease progression, and the effects of therapies that reduce proteinuria on dyslipidemias. Systematic searches for all studies on dyslipidemia prevalence, association with

atherosclerotic cardiovascular disease, and treatment for patients with Stages 1–4 CKD were not conducted. As described in the guideline document, the Work Group concluded a priori that the Adult Treatment Panel III (ATP III) Guidelines were generally applicable to patients with Stages 1–4 CKD.

Briefly, the literature search included only full, peer-reviewed, journal articles of original data. Review articles, editorials, letters, case studies, and abstracts were excluded. Studies were identified primarily through MEDLINE searches of the English language literature up to May 2001. Studies published between May 2001 and November 2002, which were identified through means other than the systematic literature searches, were included if appropriate.

Separate search strategies were developed for each topic. The text words or Medical Subject Headings (MeSH) for all topics included kidney or kidney diseases, hemodialysis, peritoneal dialysis, or kidney transplant. The searches were limited to human studies, but included both adult and pediatric populations. Potential articles for retrieval were identified from printed abstracts and titles, based on study population, relevance to the topic, and article type. These were screened by clinicians on the Evidence Review Team. Overall, 10,363 abstracts were screened, 642 articles were retrieved, and 258 articles were subjected to structured review by members of the Work Group. Although systematic, manual searches were not conducted, members of the Work Group supplied a number of articles that were not located by the MEDLINE searches.

NUMBER OF SOURCE DOCUMENTS

Abstracts screened = 10,363

Articles retrieved = 642

Articles reviewed = 258

Formal structured review of content and methodology = 133

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The strength of evidence was assessed using a rating system that takes into account (1) methodological quality of the studies; (2) whether or not the study was carried out in the target population, i.e., patients with chronic kidney disease (CKD), or in other populations; and (3) whether the studies examined health outcomes directly, or examined surrogate measures for those outcomes, e.g., improving dyslipidemia rather than reducing cardiovascular disease (see Table 8 in the original guideline document). These 3 separate study characteristics were combined in rating the strength of evidence provided by pertinent studies.

Rating the Strength of the Evidence

Strong
Evidence includes results from well-designed, well-conducted study/studies in the target population that directly assess effects on net health outcomes.

Moderate
Evidence is sufficient to determine effects on net health outcomes in the target population, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; OR evidence is from a population other than the target population, but from well-designed, well-conducted studies; OR evidence is from studies with some problem in design and/or analysis; OR evidence is from well-designed, well-conducted studies on surrogate endpoints for efficacy and/or safety in the target population.

Weak
Evidence is insufficient to assess the effects on net health outcomes because it is from studies with some problems in design and/or analysis on surrogate endpoints for efficacy and/or safety in the target population; OR the evidence is only for surrogate measures in a population other than the target population; OR the evidence is from studies that are poorly designed and/or analyzed.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data extraction forms were designed to capture information on various aspects of the primary articles. Forms for all topics included study setting and demographics, eligibility criteria, causes of kidney disease, numbers of subjects, study design, study funding source, population category (see Appendix 1 in the original guideline document), study quality (based on criteria appropriate for each study design; see Appendix 1 in the original guideline document), appropriate selection and definition of measures, results, and sections for comments and assessment of biases. Training of the Work Group members to extract data from primary articles subsequently occurred by e-mail as well as at meetings.

The Evidence Review Team used the information from these forms to construct the Evidence Tables.

Two types of evidence tables were prepared. Detailed tables contain data from each field of the components of the data extraction forms. These tables are contained in the Evidence Report, but are not included in the guideline manuscript. Summary tables describe the strength of evidence according to four dimensions: study size, applicability depending on the type of study subjects, methodological quality, and results. Within each table, studies are ordered first by methodological quality (best to worst), then by applicability (most to least), and then by study size (largest to smallest). Refer to Appendix 1 in the original guideline for details.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guidelines were developed using an evidence-based approach similar to that endorsed by the Agency for Health-Care Research and Quality. The Work Group members were the principal reviewers of the literature, and, from these detailed reviews, they summarized the available evidence and took the primary roles of writing the guidelines and rationale statements.

The Work Group and Evidence Review Team developed (a) draft guideline statements, (b) draft rationale statements that summarized the expected pertinent evidence, (c) mock summary tables containing the expected evidence, and (d) data extraction forms requesting the data elements to be retrieved from the primary articles to complete the tables. The development process included creation of initial mock-ups by the Work Group Chair and Evidence Review Team followed by iterative refinement by the Work Group members. The refinement process began prior to literature retrieval and continued through the start of reviewing individual articles. The refinement occurred by e-mail, telephone, and in-person communication regularly with local experts and with all experts during in-person meetings of the Evidence Review Team and Work Group members.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating the Strength of Recommendations

A
It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is strong evidence that the practice improves net health outcomes.

B
It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderate evidence that the practice improves health outcomes.

C
It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence, poor evidence, or the opinions of the Work Group and reviewers that the practice might improve net health outcomes.

Health outcomes are health-related events, conditions, or symptoms that can be perceived by individuals to have an important effect on their lives. Improving net health outcomes implies that benefits outweigh any adverse effects.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines underwent widespread critical review before they were finalized.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the Recommendations Ratings (A-C) are provided at the end of the "Major Recommendations" field.

Assessment of Dyslipidemias

Guideline 1
1.1. All adults and adolescents with chronic kidney disease (CKD) should be evaluated for dyslipidemias. (B)

1.2. For adults and adolescents with CKD, the assessment of dyslipidemias should include a complete fasting lipid profile with total cholesterol, low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), and triglycerides. (B)

1.3. For adults and adolescents with Stage 5 CKD, dyslipidemias should be evaluated upon presentation (when the patient is stable), at 2–3 months after a change in treatment or other conditions known to cause dyslipidemias; and at least annually thereafter. (B)

Guideline 2
2.1. For adults and adolescents with Stage 5 CKD, a complete lipid profile should be measured after an overnight fast whenever possible. (B)

2.2. Hemodialysis patients should have lipid profiles measured either before dialysis or on days not receiving dialysis. (B)

Guideline 3
Stage 5 CKD patients with dyslipidemias should be evaluated for remediable, secondary causes. (B)

Treatment of Adults with Dyslipidemias

Guideline 4
4.1. For adults with Stage 5 CKD and fasting triglycerides $\geq$500 mg/dL ($\geq$5.65 mmol/L) that cannot be corrected by removing an underlying cause, treatment with therapeutic lifestyle changes (TLC) and a triglyceride-lowering agent should be considered. (C)

4.2. For adults with Stage 5 CKD and LDL ≥100 mg/dL (≥2.59 mmol/L), treatment should be considered to reduce LDL to <100 mg/dL (<2.59 mmol/L). (B)

4.3. For adults with Stage 5 CKD and LDL <100 mg/dL (<2.59 mmol/L), fasting triglycerides ≥200 mg/dL (≥2.26 mmol/L), and non-HDL cholesterol (total cholesterol minus HDL) ≥130 mg/dL (≥3.36 mmol/L), treatment should be considered to reduce non-HDL cholesterol to <130 mg/dL (<3.36 mmol/L). (C)

Treatment of Adolescents with Dyslipidemias

Guideline 5
5.1. For adolescents with Stage 5 CKD and fasting triglycerides ≥500 mg/dL (≥5.65 mmol/L) that cannot be corrected by removing an underlying cause, treatment with therapeutic lifestyle changes (TLC) should be considered. (C)

5.2. For adolescents with Stage 5 CKD and LDL ≥130 mg/dL (≥3.36 mmol/L), treatment should be considered to reduce LDL to <130 mg/dL (<3.36 mmol/L). (C)

5.3. For adolescents with Stage 5 CKD and LDL <130 mg/dL (<3.36 mmol/L), fasting triglycerides ≥200 mg/dL (≥2.26 mmol/L), and non-HDL cholesterol (total cholesterol minus HDL) ≥160 mg/dL (≥4.14 mmol/L), treatment should be considered to reduce non-HDL cholesterol to <160 mg/dL (<4.14 mmol/L). (C)

Definitions

Recommendations Rating Scheme:

A
It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is strong evidence that the practice improves net health outcomes.

B
It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderate evidence that the practice improves health outcomes.

C
It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence, poor evidence, or on the opinions of the Work Group and reviewers, that the practice might improve net health outcomes.

Health outcomes are health-related events, conditions, or symptoms that can be perceived by individuals to have an important effect on their lives. Improving net health outcomes implies that benefits outweigh any adverse effects.

CLINICAL ALGORITHM(S)

The following clinical algorithms are provided in the original guideline document:

- The approach to treatment of dyslipidemias in adults with chronic kidney disease
- The approach to treatment of dyslipidemias in adolescents with chronic kidney disease

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Assessment of Dyslipidemias

To ascertain the prevalence of dyslipidemias in chronic kidney disease (CKD), the Work Group and Evidence Review Team examined retrospective and prospective cohort studies. To ascertain the association between dyslipidemias and atherosclerotic cardiovascular disease or CKD progression, the Work Group and Evidence Review Team examined retrospective and prospective cohort studies, as well as case-control studies.

Treatment of Dyslipidemias

Evidence supporting guideline statements regarding the efficacy of treatment of dyslipidemias was sought only in randomized controlled trials of patients with CKD. Direct and indirect evidence on the safety of treatment of dyslipidemias in CKD was sought in controlled and uncontrolled studies of (1) the pharmacokinetics of lipid-lowering medications in CKD; (2) possible drug interactions in CKD; and (3) possible adverse reactions to lipid-lowering therapies in CKD (including small series and case reports).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Dyslipidemias are very common in the target population (adults and adolescents with Stage 5 chronic kidney disease [CKD], and kidney transplant recipients), but no randomized controlled trials have examined the effects of dyslipidemia treatment on cardiovascular disease (CVD). Nevertheless, evidence from the general population suggests that treatment of dyslipidemias reduces cardiovascular disease, and evidence in patients with Stage 5 CKD suggests that judicious treatment can be safe and effective in improving dyslipidemias.
- Refer to the original guideline document where the guideline developers weigh the potential benefits and risks of treatment interventions in patients with CKD and dyslipidemia, and provide additional details regarding the management of these patients.

POTENTIAL HARMS

- The Adult Treatment Panel III (ATP III) suggests that a cautious approach be taken to dyslipidemias in chronic kidney disease (CKD), because these

persons are prone to drug side effects (e.g., they are at increased risk for myopathy from both fibrates and statins).
- Refer to the original guideline document where the guideline developers weigh the potential benefits and risks of treatment interventions in patients with CKD and dyslipidemia, and provide additional details regarding the management of these patients.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Statins are contraindicated in patients with liver disease.
- Bile acid sequestrants are contraindicated in adult patients with triglycerides >400 mg/dL (>4.52 mmol/L) in adults and ≥500 mg/dL (≥5.65 mmol/L) in children and adolescents, since they may increase triglycerides in some patients. They are relatively contraindicated for triglycerides >200 mg/dL (2.26 mmol/L) in children and adults.
- Contraindications to nicotinic acid include liver disease, severe gout, and active peptic ulcer disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care, and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.
- Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health-care professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Kidney Foundation. Clinical practice guidelines for managing dyslipidemias in chronic kidney disease. Am J Kidney Dis 2003 Apr;41(4 Suppl 3):S1-91. [452 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Apr

GUIDELINE DEVELOPER(S)

National Kidney Foundation - Disease Specific Society

SOURCE(S) OF FUNDING

The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) supported by an unrestricted educational grant from Amgen, Inc., for launching the guidelines and for continued work since 2000; and by unrestricted funds from Fujisawa Healthcare, Inc. as the primary sponsor of the present set of guidelines.

GUIDELINE COMMITTEE

National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) Clinical Practice Guidelines for Managing Dyslipidemias in Chronic Kidney Disease Work Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Work Group Members: Bertram Kasiske, MD (Chair); Fernando G. Cosio, MD (Vice-Chair); Judith Beto, PhD, RN, FADA; Blanche Chavers, MD; Richard Grimm, Jr, MD, PhD; Adeera Levin, MD, FRCPC; Bassem Masri, MD; Rulan Parekh, MD, MS; Christoph Wanner, MD; David Wheeler, MD, MRCP; Peter Wilson, MD

Liaison Member: Kline Bolton, MD, FACP (RPA)

Methodology Consultants: Joseph Lau, MD, (Director); Vaidyanatha Balakrishnan, MD, PhD; Bruce Kupelnick, BA; Caroline McFadden, MD; Kimberly Miller, BA

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Bertram Kasiske, MD, FACP, (Work Group Chair) has a research grant from Merck; has lectured for Roche, Novartis, Wyeth, and Fujisawa; and has been a consultant to Wyeth and Novartis.

Fernando G. Cosio, MD, (Work Group Vice-Chair) has received grants from the Juvenile Diabetes Foundation and the National Kidney Foundation of Ohio.

Judith Beto, PhD, RD, FADA, has received grants from the National Kidney Foundation's Council on Renal Nutrition, the American Dietetic Association Foundation, and Dominican University, and is on the Scientific Advisory Board of R&D Laboratory, Marina del Ray, California.

Kline Bolton, MD, FACP, serves on the Advisory Boards for Amgen and Ortho-Biotech.

Blanche M. Chavers, MD, has received grants from the Department of Health and Human Services for the National Health and Nutrition Survey IV (NHANES), the US Renal Data System, and Roche Global Development.

Richard Grimm, Jr, MD, PhD, has received research funds or grants from Pfizer, Bristol-Myers Squibb, Merck, AstraZeneca, and Solvay.

Adeera Levin, MD, FRCPC, is on the Medical Advisory Board of Amgen Canada and Amgen USA, as well as Janssen Cilag International, Ortho Biotech Inc., Canada, and Roche International. She has received grants from the Kidney Foundation of Canada, BC Health Research Foundation, BC Transplant Foundation, Janssen Cilag International, Ortho Biotech, Amgen, and Genzyme, Inc.

Bassem Masri, MD, has received research funding from the National Institutes of Health as well as from Merck, AstraZeneca, Bristol-Myers Squibb, Sankyo, and Smith Kline Beecham (now GlaxoSmithKline).

Rulan Parekh, MD, MS, has received research funding from the Child Health Center of the National Institutes of Health, The Thomas Wilson Sanitarium, and the National Kidney Foundation of Maryland. She currently receives funding from the National Institutes of Diabetes and Digestive Disease (NIDDK) of the NIH.

Christoph Wanner, MD, has received research grants from Pfizer and Fresenius Medical Care (FMC) and lecture fees from Aventis, Roche, Merck, Janssen-Cilag, and FMC.

David C. Wheeler, MD, FRCP, currently receives research funding from the UK National Kidney Research Fund, the British Heart Foundation, the British Renal Society, and the Baxter Healthcare Extramural Grant Program. He has also received research funding from Merck and Amgen, has undertaken consultancy work for Fresenius, serves on the UK and European Advisory Boards of Genzyme, and has been paid lecture fees by Bristol-Myers Squibb, Novartis, Wyeth, and Fujisawa.

Peter W.F. Wilson, MD, has received research support from Roche Laboratories and served as a consultant to Lilly, Bayer, Bristol-Myers Squibb, Merck, Novartis, Pfizer, and Roche. He has also been a speaker for Merck, Pfizer, and Roche.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) Web site.

Print copies: Available from the National Kidney Foundation (NKF), 30 East 33rd St., New York, NY 10016.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Guideline Development and Methodology. New York (NY): National Kidney Foundation (NKF), 2003.

Electronic copies: Available from the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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